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Reproductive and Developmental Effects in Mammalian and Avian Species from Exposure to Elf (Extremely Low Frequency Fields)

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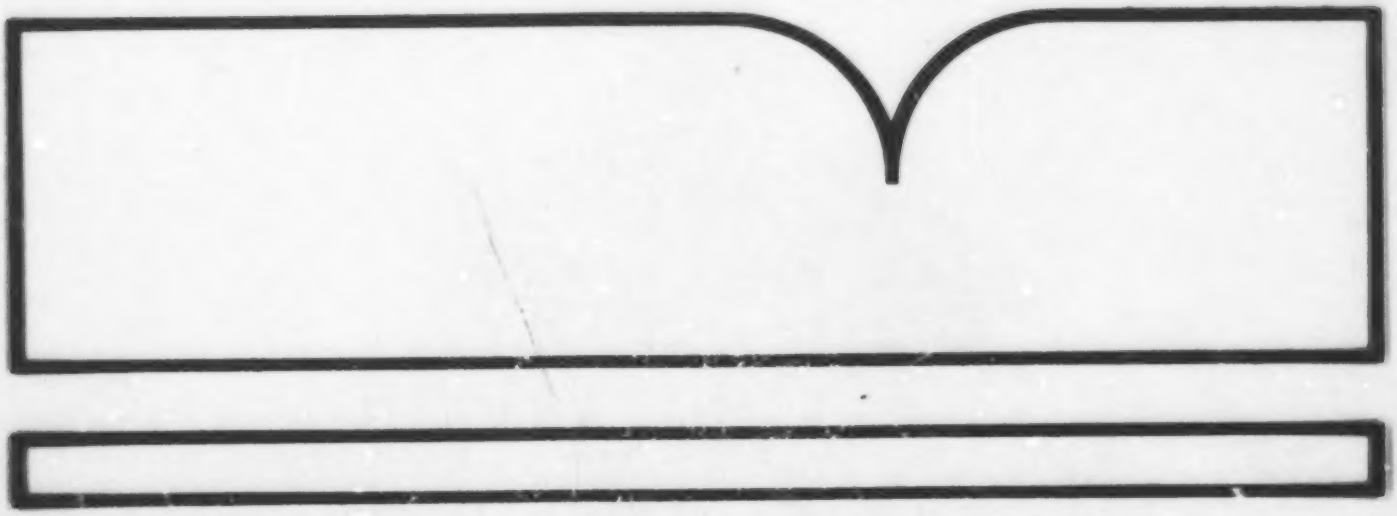

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REPRODUCTIVE AND DEVELOPMENTAL EFFECTS IN MAMMALIAN AND AVIAN SPECIES FROM EXPOSURE TO ELF FIELDS

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16. ABSTRACT

This paper critically reviews the Extremely Low Frequency (ELF) Electromagnetic Fields literature from 1978 to the present in regard to research dealing with the reproductive and developmental effects of expsoure.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field Group

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INTRODUCTION: The normal development, growth, and maturation of an organism is brought about by a complex series of interrelated genetic, biochemical, and morphological events occurring in a precise temporal sequence. It has been long established that substantive interference with any of the key events involved in development may have serious sequelae; embryonic or fetal death, the occurrence of terata (birth defects), failure to thrive postnatally (or posthatching) or failure to reproduce. A diverse series of agents including disease, drugs, environmental chemicals, and physical agents such as x-irradiation are known to have produced serious effects in humans (Wilson, 1973). Because of this known sensitivity, the scientific community has been called upon to devise and accomplish studies in laboratory species which will indicate any special sensitivity of developmental processes to specific external influences. A number of studies whose purpose was to evaluate the potential developmental toxicity of ELF electric and/or magnetic radiation have been reported from 1976 to the present. The following review centers upon those studies in which mammalian or avian species were exposed to ELF electric and magnetic radiation, and effects on subsequent growth and/or development were monitored. The review is divided into those studies which utilized electric fields with frequencies of 50- or 60-Hz at intensities simulating those found in the vicinity of power lines, and those studies which utilized low-intensity magnetic fields.

STUDIES WITH 50- or 60-Hz ELECTRIC FIELDS:

A. Avian species. Graves (1984) reported on a series of experiments in which chicken eggs and/or hatched chicks were exposed to 60-Hz electric fields ranging from 0.1 to 100 kV/m. Eggs were checked for embryotoxic

effects including teratogenicity on incubation days 7 or 14. Other groups were exposed during the first 19 days in ovo, allowed to hatch (generally on day 20 or 21) and the emerging chicks monitored for changes in growth, viability, or behavioral alterations during a six week period after hatching. There were no significant dose-related effects found in any parameters studied; those statistically significant effects which were noted appear to be random in nature. The author's conclusion that these studies produced "no consistent direct effect of 60-Hz electric fields on processes associated with growth, development, and overall health and well-being of avian embryos" is an accurate interpretation of the data. In another series of experiments Graves et al. (1978) exposed chicks postnatally to either 30 minute or 3 week exposures of 60-Hz fields (40 or 80 kV/m) and monitored growth and livability. No effects were noted with short-term exposure. Long-term exposure resulted in a slight enhancement of growth in male birds through day 16 posthatching. This effect was not seen in female birds. The authors also recorded the EEG's and ECG's of chicks immediately after removal from the field and found no differences.

B. Mammalian Species - A variety of species have been used in experiments to evaluate the potential effects of electromagnetic fields of growth and/or development. Such species have included the rat, mouse, guinea pig, and swine. Adrienko (1977) studied the effects of 50-Hz fields of 5 kV/m on rats of unkown strain before, during, and after embryo/fetal development. Male and female rats were exposed for 1 1/2, 3 1/2, and 4 1/2 months and examined. An additional group was allowed to recover for 1 month and then examined. The author reports numerous effects of the fields

on the offspring of both exposed male and females. Close examination of the data raises questions which are impossible to resolve, however. The author presents postnatal death as % ± (std. dev) and this data is difficult to understand since the standard deviations are extremely low for this type of presentation (ie. 4.3 ± 0.008 or 14.8 ± 0.2). Data presented as % invariably have larger standard deviations than those presented in this paper. It is difficult to interpret some of the data biologically: After 1 1/2 months of exposure there are no differences in breeding efficiency; at 3 1/2 months treated females were affected, and at 4 1/2 months only treated males were affected. In general, however, the weight of the newborn pups and their viability at 21 days is reduced in litters of both treated males and females. The author does not offer any biological explanation for the male-mediated effect which resulted in such relatively slight effects. Male-mediated effects usually result in embryonic lethality and in these studies there was no reduction in litter size in any of the treated groups. The author also report that reproductive function was adversely affected in both treated females (an altered cyclicity and ovarian histopathology) and males (a decrease in sperm number and in testicular histopathology). Cerritelli et al. (1979) studied a variety of biological phenomona in diverse species exposed to 50-Hz electric fields at 10, 25, and 100 kV/m. The experiments which focused on the developmental effects in rats are somewhat difficult to interpret. The growth rates were reported to be decreased in the 25 and 100 kV/m groups but the age of the rats was not specified. In addition, although the authors report food intake values, they do not provide information on water intake. Male reproductive function was measured but some of the parameters are again difficult to interpret. There is no explanation as

to how the number of copulations may be using the methodologies employed. No description is given of the microscopic alterations found after examination of testes tissue. No indication is given as to how the "vitality" of sperm is measured. The authors conclude that fertility was not affected and the treatment was not teratogenic although they did see a reduction in fetal weight (data not given). Free et al. (1981) examined the effects of 60-Hz electric fields at 64 kV/m (effective field strength) on endocrine profiles of Sprague-Dawley rats exposed for 7 weeks starting at 20 days of age. Testosterone, FSH, LH, corticosterone, prolactin, TSH, GS, and thyroxine were monitored in addition to the body and organ weights. The experiments were repeated in the same month in three consecutive years. Data were not consistent from year to year with the exception of testosterone levels which were reduced when compared to the controls in all three years. A key difficulty in such work is pointed out by the authors - that of examining cyclical hormone levels at specific time points, and they suggest that some of the changes noted may have been due to alterations in the hormone cycles. Margonato and Viola (1982) studied the offspring of male rats exposed to 50-Hz (100 kV/m) either for short periods (30 minutes/day) or longer periods (8 hours/day) for up to 48 days. No consistent effects in fertility, sperm viability or sperm morphology were noted in any of the exposed groups. There were no treatment-related effects in the number of implantations, % live fetuses, or incidence of malformations. The authors conclude that there were no significant treatment-related effects on male reproductive parameters. A series of studies were performed by Sikov et al. (1984) in which the effects of 60-Hz electric fields (65 kV/m effective) on prenatal and postnatal

development in Sprague-Dawley rats were investigated. Experiments were designed to test reproductive performance and prenatal development, postnatal sequelae of exposure throughout gestation and the first week postpartum, and postnatal effects of late gestation and 25 days postnatal exposure. There were no consistent treatment-related effects noted in any of the parameters studied. Fetal development was unaffected as was postnatal growth, viability, and the development of reflexes. Seto et al. (1981) reported in an abstract that the chronic exposure of rats to 60-Hz, 20 kV/m electric fields for four generations did not affect organ weights or histological parameters of selected organs. Burack et al. (1981) presented data in an abstract which reported a study of the effects of 60-Hz (80 kV/m) electric fields on the offspring of rats exposed from days 14-21 of gestation. Group sizes were small (seven animals per group) and no significant changes were detected in litter size or viability. The authors state that exposed offspring were generally of lighter body weight and had delayed ear flap and eye opening.

The mouse has also been used by a number of investigators to study the effects of electric fields on development. Marino et al. (1976) reported studies in which ICR mice were exposed for 3 generations (60-Hz, 15 kV/m vertical or 10 kV/m horizontal electric field). The vertical field reduced litter weights in all generations and the horizontal field had a similar effect on the first two generations. These studies were compromised by the potential presence of substantial grounding microcurrents which would affect the eating and/or drinking behavior of the exposed animals. This same group repeated these studies in an improved apparatus which was designed so that grounding microcurrents would not be present (Marino et al. 1980). Animals were exposed to 60-Hz electric fields

with either horizontal or vertical strengths of 3.5 kV/m. The results are variable and in some cases (e.g. growth) the opposite of that seen in the first experiment. The authors state that increased preweanling and/or postweanling mortality occurred in some generations. They attribute the variablity inconsistencies to generalized stress caused by the exposures. Fam (1980) exposed male and female ICR-SW mice to 240 kV/m, 60-Hz electric fields throughout the entire developmental period. Animals were bred and the resultant litters monitored for growth, histology and biochemical parameters of the blood, and histology of critical organs. Drinking water consumption of the parental animals was depressed and the growth (between 53 and 123 days of age) of the females was significantly reduced during the exposure period. No changes were noted in the number, growth, or survival of the offspring.

Two studies utilizing the swine have been reported. Mahmoud and Zimmerman (1982) reported on the growth of pigs (average age at initiation of experiment was 79 days) housed under a 60-Hz, 345 kV power line. No significant differences were noted between the growth of the animals exposed to 3.5-4.2 kV/m intensity and those housed one half mile from the line. A multigeneration study was done with Hanford miniature swine which were continuously exposed to a vertical electric field (60-Hz, 30 kV/m) (Sikov et al., 1983). Animals were exposed for four months and then bred, some being sacrificied to allow for fetal evaluation and other allowed to go term. After 10 months the remaining dams were again bred and their fetuses underwent examination. The young that had been born to the parent generation were, in turn, breed at 18 months, allowed to litter normally, and then bred 10 months later, sacrificed, and their

fetuses evaluated. There were thus a total of three teratology series and two groups of live births. The data generated in these studies was highly variable across generations, and although there was a significant increase in malformations in the exposed litters of the second breeding of the F_0 generation, these results were not seen in the first breeding of the F_0 generation. It was also seen in the first litters of the F_1 generation. It should be noted that the types of defects seen were of a wide spectrum and there was no apparent specific morphological pattern that occurred throughout these studies. These studies fail, therefore, to present clear evidence of a treatment-related effect although such a possibility cannot be ruled out.

Sasser et al. (1984) studied the effects of electric field exposure on the prenatal development of the guinea pig (Duncan-Hartley strain). Experimental animals (females) were exposed to 60-Hz electric fields (100 kV/m) for forty days, bred and allowed to litter. The parental animals were bred a second time; however, this portion of the experiment was terminated prematurely due to physical plant problems so that the results are difficult to intepret. Results of the first breeding indicate no statistically significant adverse effects in terms of pregnancy rate, precent dams which aborted/resorbed, or number of litters with stillborns. There were also no differences noted in pups at birth in terms of avg. litter size or birth weight. No significant incidences of terata were noted in these groups.

STUDIES WITH MAGNETIC FIELDS:

A. Avian species. Delgado et al. (1982) exposed chicken eggs for 48 hours immediately after hatching to pulsed magnetic fields (10, 100 or

1000-Hz at repetition frequencies of 0.12, 1.2, or 12 μT). There were 9 dose groups (42 eggs total) plus a control group (26 eggs). The embryos were harvested after the exposure period, preserved, and examined for both morphological and histological anomalies. The criteria for normality used by the authors was embryological development to stages 11-12 of Hamburger and Hamilton (1951). The embryo exposed to 10-Hz were almost all normal. At 100 and 1000-Hz, however, exposed embryos were significantly retarded (equivalent to Stage 6 of Hamburger and Hamilton) at all intensities tested. Histological analyses confirmed the results noted after gross examination. The numbers of embryos used in the study are small ranging from 3 to 9 per group and although the authors refer to statistical signficances, no p-Values or methodologies are given. It would appear, however, that growth retardation did occur in the exposed eggs. The same group of workers reported on additional studies with chicken eggs in which four different pulse types were used at different intensities (Ubeda et al. 1983). The results are extremely difficult to interpret. Using pulses which had rise and fall times of 100 μ sec, an increase in abnormalities was seen at 1.0 μT but not at 0.4, 10.4, 13.9 or 104.0 μT. There were six replicates in which embryos were exposed to 1.0 μT, and although there was a constant trend towards a greater effect in exposed eggs, it was also apparent that both control and exposed eggs varied widely in the percentages of abnormalities noted from replicate to replicate (56% abnormalities in replicate 1 controls vs 0% ties in replicate 3). Furthermore, it is apparent that the percentage of abnormalities followed the same overall replicate pattern in both controls and exposed

eggs. The authors considered positive effects to be associated with specific pulse shapes as they found effects with pulse B which had fast rise and fall times of 2 μ sec (at 0.4 μ T), and with pulse D which had 42 μ sec rise and fall times and was without ripple during the on period (1.0 μ), but not with pulse C which was identical to pulse D except for a ripple during the on period (1.0 μ T). Embryos exposed to pulse B were more advanced than concurrent controls. This is an extremely unusual finding since embryonic toxicity almost always is manifested as growth retardation. The authors did note that in pulse D experiments there was a retardation of development in exposed embryos compared to controls. To adequately interpret these data, information on the temperatures in the incubation chambers must be given such differences may affect the relative rates of development.

B. Mammalian Studies. Fam (1981) exposed male SW-ICR mice to a 60-Hz, 0.11 T alternating magnetic field for a period of one week. Exposed animals tended to lose weight although their water consumption was increased relative to controls. No significant differences between treated and untreated animals were noted in blood counts, blood proteins or critical organ histology. A reproductive study was performed on one control and one exposed mouse but data derived from n's of this size cannot be interpreted.

Persinger et al. (1978) exposed pregnant Wister rats to one of three treatments (a 0.5-Hz rotating magnetic field at 5, 100, or 1000 μ T) from day 19 of gestation to 3 days postpartum. Group sizes were small (three animals per group). Pups were sacrificed after weaning and some 20 blood serum parameters were measured. The differences noted appear to be random, having as much to do with the type of housing (plastic vs

metal caging) as with the exposure conditions.

Grisset et al. (1979) exposed rhesus monkeys (ages unspecified) to a magnetic field of 0.2 mT and simultaneously to an electric field of 20 V/m. These fields were alternating at approximately 76-Hz. The animals were monitored for growth rate and blood chemistry, and (in the third year) for spermatogenesis. The only differences which was seen consisted of an increased growth rate in male animals during the first year of exposure. Sham and exposed animals were matched for weight rather than for age so that it is possible that the differences noted were due to an inadvertent difference in the growth rate of exposed and sham animals at the beginning of the experiments (a point which the author himself raises). Using the same exposure regimen the authors published an abstract Grisset et al. (1981) reporting a similar experiment using younger animals. In this study no differences in growth and development were noted in animals exposed from four to 67 weeks of age indicating that the fields did not cause a general enhanced growth rate.

SUMMARY: The adequate evaluation of studies investigating potential developmental toxicology requires three critical components. The first is a demonstrable compoundrelated effect. Studies must utilize sufficient numbers of experimental animals to insure a maximum probability of a real effect being found. Concurrent controls must be run under conditions that assure that the only variable being tested is the agent of concern. Rigorous and appropriate statistical analyses must be performed. This latter is especially critical for studies in which a large number of agents and/or endpoints are being investigated since such analyses help

identify differences due to normal random biological variation. The second important factor is the presence of a dose-response relationship. If a given chemical has a reported effect at x mg/kg., one expect that x + y mg/kg will produce either a similar effect (if the system is saturated) or a greater effect (either quantitatively or qualitatively). Most toxicity bioassays are therefore run with multiple dose levels and the presence of a real dose-response relationship is one of the strongest evidences of the validity of the reported effect. Finally, a key component of any evaluation of an agent is the replicability of the effect. Experimental parameters must be defined with sufficient rigor so as to allow other scientists to produce similar results in replicate experiments. It is impossible to draw definitive conclusions from a study which cannot be replicated until the reason for this lack is fully documented.

Given the criteria listed above, it is impossible to draw any definitive conclusions concerning the effects of ELF fields of reproduction and/or development in either avian or mammalian studies. While there are a number of studies which have reported possible agent-related findings, few of these studies have dealt with dose-response phenomona and none have been clearly replicated by different research groups. Studies on possible effects of 50 or 60-Hz electric fields on mammals range from the positive effects of Adrienko (1977) with the rat, and Marino (1981) with the mouse to the negative findings by Margonato and Viola (1982) and Sikov (1984) with the rat, and Fam (1980) and Smith et al. (1981) with the mouse. Studies with swine have internal variability which prevents firm conclusions from being drawn, but the data certainly do not indicate definitive adverse effects due to ELF exposure. The

studies which have been done with the guinea pig (Sasser et al. 1984) appear to be negative as do those studies which employed avian species Graves (1984).

The exposure of mammalian species to magnetic fields indicate a possible increased growth rate Grisset et al. (1979) but the experimental design does not allow for definite conclusions on this point. In avian species, studies have indicated that such fields produce adverse effects Delgado et al. (1984), Ubeda et al. (1983) but the nature of the internal variability and lack of dose-response data in these studies again does not allow for definitive conclusions.

In summary, therefore, ELF fields have not been demonstrated to produce adverse reproductive and/or developmental effects in either mammalian or avian species. There are a small number of studies (especially with magnetic field) which suggest some agent-related effects but these studies must be replicated before any definitive statements can be made.

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